



## Clinical trial results:

### A Multi-center, Randomized, Open-Label, Parallel-Group Study with LJPC-401 for the Treatment of Myocardial Iron Overload in Patients with Transfusion-Dependent Beta Thalassemia

#### Summary

EudraCT number	2017-003372-31
Trial protocol	GB GR CY IT
Global end of trial date	14 January 2020

#### Results information

Result version number	v1 (current)
This version publication date	08 May 2022
First version publication date	08 May 2022

#### Trial information

##### Trial identification

Sponsor protocol code	LJ401-BT01
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03381833
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	La Jolla Pharmaceutical Company
Sponsor organisation address	4747 Executive Drive, Suite 240, San Diego, United States, 92121
Public contact	Regulatory Affairs, La Jolla Pharmaceutical Company, 1 831-421-1450, meddleman@ljpc.com
Scientific contact	Regulatory Affairs, La Jolla Pharmaceutical Company, 1 831-421-1450, meddleman@ljpc.com

Notes:

##### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 October 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 November 2019
Global end of trial reached?	Yes
Global end of trial date	14 January 2020
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

Efficacy on cardiac iron as measured by cardiac T2\* MRI in patients with transfusion-dependent beta thalassemia

Protection of trial subjects:

The study was conducted in accordance with the ethical principles founded in the Declaration of Helsinki and in compliance with the protocol, the International Council on Harmonisation (ICH) for Good Clinical Practice (GCP) and the appropriate regulatory requirements.

The study was conducted in accordance with the ICH E6 GCP for obtaining informed consent. Each patient provided written informed consent after the study was fully explained and before any study-specific procedures (including study-specific screening procedures) were performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Greece: 9
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Lebanon: 13
Country: Number of subjects enrolled	Thailand: 4
Country: Number of subjects enrolled	Turkey: 29
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	84
EEA total number of subjects	21

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	84
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Patients were screened to ensure they were clinically diagnosed with beta thalassemia for which they were transfusion-dependent and had myocardial iron overload. Patients were to be 14 years or older with a cardiac T2\* MRI of 6 to 35 msec.

### Period 1

Period 1 title	Period 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Group A

Arm description:

Group A did not receive treatment other than Standard of Care during Period 1. During Period 2, Group A received 10 mg BIW LJPC-401 plus Standard of Care.

Arm type	Standard of Care
Investigational medicinal product name	LJPC-401
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Week 1 through 26 (Period 1): SOC Only

Week 27 through Week 52 (Period 2): LJPC-401 10 mg Bi-weekly plus SOC.

Doses were given as one or more intramuscular injections. If more than one injection was needed, injections were spread over different parts of the body.

<b>Arm title</b>	Group B
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Arm description:

Group B received 5-20 mg LJPC-401 QW plus Standard of Care.

Arm type	Experimental
Investigational medicinal product name	LJPC-401
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

The dose level in Group B was escalated the first 3 weeks of Period 1 per the following schedule:

Week 1 (Period 1): LJPC-401 5 mg QW and SOC

Week 2 (Period 1): LJPC-401 10 mg QW and SOC

Week 3 through Week 52 (Period 1 through Period 2): LJPC-401 20 mg QW and SOC

Doses were given as one or more intramuscular injections. If more than one injection was needed, injections were spread over different parts of the body.

<b>Number of subjects in period 1</b>	Group A	Group B
Started	42	42
Completed	26	26
Not completed	16	16
Consent withdrawn by subject	-	3
Physician decision	-	1
Adverse event, non-fatal	-	1
Pregnancy	1	-
Sponsor Decision	15	11

## Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Group A

#### Arm description:

Group A did not receive treatment other than Standard of Care during Period 1. During Period 2, Group A received 10 mg BIW LJPC-401 plus Standard of Care.

Arm type	Standard of Care
Investigational medicinal product name	LJPC-401
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

#### Dosage and administration details:

Week 1 through 26 (Period 1): SOC Only

Week 27 through Week 52 (Period 2): LJPC-401 10 mg Bi-weekly plus SOC.

Doses were given as one or more intramuscular injections. If more than one injection was needed, injections were spread over different parts of the body.

<b>Arm title</b>	Group B
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#### Arm description:

Group B received 5-20 mg LJPC-401 QW plus Standard of Care.

Arm type	Experimental
Investigational medicinal product name	LJPC-401
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

#### Dosage and administration details:

The dose level in Group B was escalated the first 3 weeks of Period 1 per the following schedule:

Week 1 (Period 1): LJPC-401 5 mg QW and SOC

Week 2 (Period 1): LJPC-401 10 mg QW and SOC

Week 3 through Week 52 (Period 1 through Period 2): LJPC-401 20 mg QW and SOC

Doses were given as one or more intramuscular injections. If more than one injection was needed, injections were spread over different parts of the body.

<b>Number of subjects in period 2</b>	Group A	Group B
Started	26	26
Completed	15	17
Not completed	11	9
Consent withdrawn by subject	4	2
Physician decision	-	1
Sponsor Decision	7	6

## Baseline characteristics

### Reporting groups

Reporting group title	Group A
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Reporting group description:

Group A did not receive treatment other than Standard of Care during Period 1. During Period 2, Group A received 10 mg BIW LJPC-401 plus Standard of Care.

Reporting group title	Group B
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Reporting group description:

Group B received 5-20 mg LJPC-401 QW plus Standard of Care.

Reporting group values	Group A	Group B	Total
Number of subjects	42	42	84
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	42	42	84
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	24	15	39
Male	18	27	45

## End points

### End points reporting groups

Reporting group title	Group A
Reporting group description: Group A did not receive treatment other than Standard of Care during Period 1. During Period 2, Group A received 10 mg BIW LJPC-401 plus Standard of Care.	
Reporting group title	Group B
Reporting group description: Group B received 5-20 mg LJPC-401 QW plus Standard of Care.	
Reporting group title	Group A
Reporting group description: Group A did not receive treatment other than Standard of Care during Period 1. During Period 2, Group A received 10 mg BIW LJPC-401 plus Standard of Care.	
Reporting group title	Group B
Reporting group description: Group B received 5-20 mg LJPC-401 QW plus Standard of Care.	

### Primary: Cardiac T2\*MRI at Week 26

End point title	Cardiac T2*MRI at Week 26
End point description:	
End point type	Primary
End point timeframe: Week 26	

End point values	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	29		
Units: Cardiac Iron Level				
least squares mean (standard deviation)	0.67 (± 3.473)	0.45 (± 3.898)		

### Statistical analyses

Statistical analysis title	Cardiac T2* MRI Change from Baseline
Comparison groups	Group A v Group B
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8092
Method	General Linear Model

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**Secondary: Cardiac T2\*MRI at Week 52**

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End point title	Cardiac T2*MRI at Week 52
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End point description:

End point type	Secondary
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End point timeframe:

Week 52

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<b>End point values</b>	Group A	Group B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	18		
Units: Cardiac Iron Level				
least squares mean (standard deviation)	1.17 ( $\pm$ 6.106)	1.94 ( $\pm$ 4.601)		

**Statistical analyses**

<b>Statistical analysis title</b>	Cardiac T2* MRI Change from Baseline at Week 52
Comparison groups	Group A v Group B
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7436
Method	General Linear Model

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the time of consent through End of Study.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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### Reporting groups

Reporting group title	Group A
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Reporting group description:

Group A did not receive treatment other than Standard of Care during Period 1. During Period 2, Group A received 10 mg BIW LJPC-401 plus Standard of Care.

Reporting group title	Group B
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Reporting group description:

Group B received 10 mg LJPC-401 QW plus Standard of Care.

<b>Serious adverse events</b>	Group A	Group B	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 42 (7.14%)	4 / 41 (9.76%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 42 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 42 (2.38%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Adenovirus infection			
subjects affected / exposed	0 / 42 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 42 (2.38%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis			
subjects affected / exposed	0 / 42 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	1 / 42 (2.38%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	Group A	Group B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 42 (71.43%)	38 / 41 (92.68%)	
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	1 / 42 (2.38%)	4 / 41 (9.76%)	
occurrences (all)	1	4	
Cardiac disorders			
Palpitations			
subjects affected / exposed	3 / 42 (7.14%)	2 / 41 (4.88%)	
occurrences (all)	4	3	

Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 42 (2.38%)	4 / 41 (9.76%)	
occurrences (all)	1	8	
Headache			
subjects affected / exposed	7 / 42 (16.67%)	6 / 41 (14.63%)	
occurrences (all)	10	16	
Paraesthesia			
subjects affected / exposed	1 / 42 (2.38%)	3 / 41 (7.32%)	
occurrences (all)	3	4	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 42 (9.52%)	2 / 41 (4.88%)	
occurrences (all)	8	4	
Injection site erythema			
subjects affected / exposed	5 / 42 (11.90%)	10 / 41 (24.39%)	
occurrences (all)	30	81	
Injection site pain			
subjects affected / exposed	8 / 42 (19.05%)	12 / 41 (29.27%)	
occurrences (all)	37	76	
Injection site pruritus			
subjects affected / exposed	1 / 42 (2.38%)	7 / 41 (17.07%)	
occurrences (all)	1	9	
Injection site rash			
subjects affected / exposed	1 / 42 (2.38%)	3 / 41 (7.32%)	
occurrences (all)	2	6	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 42 (7.14%)	1 / 41 (2.44%)	
occurrences (all)	5	1	
Abdominal pain upper			
subjects affected / exposed	3 / 42 (7.14%)	4 / 41 (9.76%)	
occurrences (all)	4	4	
Constipation			
subjects affected / exposed	3 / 42 (7.14%)	1 / 41 (2.44%)	
occurrences (all)	4	1	

Diarrhoea			
subjects affected / exposed	7 / 42 (16.67%)	3 / 41 (7.32%)	
occurrences (all)	11	3	
Nausea			
subjects affected / exposed	2 / 42 (4.76%)	5 / 41 (12.20%)	
occurrences (all)	4	10	
Vomiting			
subjects affected / exposed	2 / 42 (4.76%)	3 / 41 (7.32%)	
occurrences (all)	5	5	
Fatigue			
subjects affected / exposed	0 / 42 (0.00%)	3 / 41 (7.32%)	
occurrences (all)	0	5	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 42 (7.14%)	5 / 41 (12.20%)	
occurrences (all)	5	6	
Nasal congestion			
subjects affected / exposed	1 / 42 (2.38%)	4 / 41 (9.76%)	
occurrences (all)	1	5	
Oropharyngeal pain			
subjects affected / exposed	3 / 42 (7.14%)	5 / 41 (12.20%)	
occurrences (all)	3	6	
Rhinorrhoea			
subjects affected / exposed	1 / 42 (2.38%)	6 / 41 (14.63%)	
occurrences (all)	1	7	
Rash			
subjects affected / exposed	1 / 42 (2.38%)	4 / 41 (9.76%)	
occurrences (all)	1	4	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	8 / 42 (19.05%)	4 / 41 (9.76%)	
occurrences (all)	10	5	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 42 (2.38%)	4 / 41 (9.76%)	
occurrences (all)	1	5	

Influenza			
subjects affected / exposed	2 / 42 (4.76%)	4 / 41 (9.76%)	
occurrences (all)	2	4	
Nasopharyngitis			
subjects affected / exposed	2 / 42 (4.76%)	3 / 41 (7.32%)	
occurrences (all)	3	3	
Sinusitis			
subjects affected / exposed	0 / 42 (0.00%)	4 / 41 (9.76%)	
occurrences (all)	0	4	
Upper respiratory tract infection			
subjects affected / exposed	10 / 42 (23.81%)	13 / 41 (31.71%)	
occurrences (all)	14	21	
Urinary tract infection			
subjects affected / exposed	0 / 42 (0.00%)	4 / 41 (9.76%)	
occurrences (all)	0	5	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 November 2017	<ul style="list-style-type: none"><li>- Revised primary endpoint</li><li>- Clarified that secondary endpoints using data from visits other than Week 26</li><li>- Updated stratification to include baseline T2* MRI results</li><li>- Added details of structure and responsibilities of the DMC</li></ul>
02 July 2018	<ul style="list-style-type: none"><li>- Clarified and expanded secondary and exploratory endpoints</li><li>- Revised LJPC-401 dosing (introduced re-randomization to two dose levels in Group A)</li><li>- PK substudy design revised</li><li>- Removed blinding from the study</li></ul>
16 November 2018	<ul style="list-style-type: none"><li>- Enrollment eligibility revised to allow patients 14 years of age and older</li><li>- Study design amended to add an additional cohort and to investigate a larger range of dosing regimens</li><li>- Revised statistical methods and analyses section to coincide with study design revisions</li><li>- Clarified that a periodic review of safety data will occur approximately every 4 months</li><li>- Interim efficacy analysis was set to occur after 20 subjects in each arm (previously 25) completed Week 26</li></ul>
20 February 2019	<ul style="list-style-type: none"><li>- Revised dosing frequencies in Period 2 for Groups A and B (study design reverted to 2 cohorts)</li><li>- Deleted previously added Group C</li><li>- Revised Group A dosage in Period 2</li><li>- Revised Group B dosage in Period 2</li></ul>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
14 January 2020	Following an interim analysis, the study was stopped early due to lack of efficacy and enrollment was discontinued. Not all the planned exploratory analyses were conducted. Analyses for the Per Protocol population were not performed.	-

Notes:

### Limitations and caveats

None reported